Original Research Article

Indian Journal of Pathology: Research and Practice
Volume 6 Number 4, October - December 2017 (Part-I)
DOI: http://dx.doi.org/10.21088/ijprp.2278.148X.6417.14

Malignant and Premalignant Lesions of the Oral Cavity: A Histopathological Study in a Rural and Semi-Urban Population of India

Prithal G.*, Priyal Rohan, Girish M.*****

*Assistant Professor, Dept. of Pathology, A.J. Institute of Medical Sciences, Mangaluru, Karnataka 575004, India, **Assistant Professor, Department of Oral Pathology, A.J. Institute of Dental Sciences, Mangaluru, Karnataka 575004, India. ***Associate Professor, Dept. of Pathology, KVG Medical College, Sullia, Karnataka 574327, India.

Abstract

Background: In a developing country like India, Oral cancer is a major health issue, representing the leading cause of death. *Objective:* Study the spectrum of premalignant and malignant lesions with grading of malignant lesions of oral cavity and to study the incidence of malignant and premalignant lesions of the oral cavity in relation to age, sex, and site of the lesion. *Methods:* The study was conducted for a period of 2 years, in the Department of Pathology, KVG Medical College and Hospital, Sullia. 100 oral biopsies received from the Surgical, Medical and Dental outpatient departments were studied. Clinical details were obtained from the requisition form. Biopsies received were processed and stained with H&E. Histopathological diagnosis regarding type and differentiation was made. Data was entered and analyzed using Microsoft excel 2007 and SPSS Version 17. Quantitative data was expressed as mean and standard deviation, Qualitative data was expressed as percentage and proportions. *Results:* Among 100 oral cavity lesions studied, 16% were premalignant and 84% were malignant lesions. Peak incidence was seen in 6th decade with a male preponderance. 43% of patients were smokers, 30% were habituated to smokeless tobacco. The commonest site in both the premalignant and malignant lesions were Buccal mucosa. Majority of cases (50%) of leukoplakias were associated with mild dysplasias, one case of erythroplakia showed mild dysplasia. Amongst the 84 malignant lesions, 78 cases were Squamous cell carcinoma and majorities (60.25%) were well differentiated. Maximum number of cases (63.63%) were seen in Stage I and II. Nodal metastasis was seen in 36.36%, perineural invasion in 27.2% and microvascular invasion was seen in 18.18% cases. Negative surgical margins were seen in 100% cases. *Conclusion and Interpretation:* A detailed clinical work up with histology can help in early detection of dysplastic and malignant changes and thus reduce morbidity and mortality due to malignant lesions.

Keywords: Erythroplakia; Leukoplakia; Squamous Cell Carcinoma; Verrucous Carcinoma.

Introduction

Owing to the major health issues in rural and semi urban population of India especially ignorance coupled with poor access to tertiary health care facilities, oral malignancies constitute one of the foremost causes of death. In the Indian subcontinent, oral malignancies accounts for about 40% of all the cancers [1]. Oral cancers have a greater potential to jeopardize the health and longevity [2]. Amongst the tumours of the oral cavity, squamous cell carcinoma is the most common malignancy and it arises from oral mucosal lining [3]. Most oral carcinomas arise within premalignant lesions. The most common premalignant lesion seen in oral cavity is leukoplakia with associated dysplasia [4].

Appropriate management of the patient with the premalignant and malignant oral lesion begins with an accurate diagnosis. Oral cavity is readily accessible for direct examination, inspite of it these malignancies are often undetected until a late stage [3]. Histopathological assessment of a tissue biopsy of suspicious lesion is the current gold standard for the diagnosis. An adequate incisional biopsy taken from the lesion can provide over 98% diagnostic accuracy as to whether the lesion is malignant or not, when routine pathological techniques are used [5].

The present study is under taken to study the

Corresponding Author: Prithal G., Assistant Professor, Department of Pathology, A.J. Institute of Medical Sciences and Research Centre, Mangaluru-575004, Karnataka, India.
E-mail: prithal@rediffmail.com

(Received on 03.08.2017, **Accepted on** 26.09.2017)

various spectrum of premalignant and malignant lesion of the oral cavity and their incidence.

Materials and Methods

A 2 years prospective study from August 2010 to August 2012 was conducted in the Department of Pathology, KVG Medical College and Hospital, Sullia, Dakshina kannada District, Karnataka. Hundred consecutive oral biopsies from patients presenting with lesions in oral cavity, received from the surgical, Medical and Dental outpatient departments were selected. Clinical details were obtained from the requisition form including age, sex, habits, clinical examination, site of biopsy, type of biopsy, and clinical diagnosis were noted.

Biopsy from the lesion were taken and were fixed in 10% neutral formalin. Thereafter the samples were processed and embedded in paraffin. 3-4µ thick sections were taken. Histopathological diagnosis was made on the H&E stained sections. The study included all the patients with lesions in the oral cavity subjected for biopsy or undergoing surgical resections at KVG Medical College and Hospital, Sullia. The study excluded Metastasis to the oral cavity from primary malignancy elsewhere in the body, Tonsils, Odontogenic tumours, recurrence after treatment of primary oral cavity malignancy, Salivary gland tumors, Soft tissue tumors, Mucosal malignant melanoma, and Hematolymphoid tumors. Data was entered and analyzed using Microsoft excel 2007 and SPSS Version 17. Quantitative data was expressed as mean and standard deviation, Qualitative data was expressed as percentage and proportions.

Results

In relation to the patients age, gender, location along with histopathological findings an incidence of premalignant and malignant lesions of oral cavity was derived. Out of 100 cases, 16 (16%) were premalignant lesions & 84 (84%) were malignant lesions. Among the premalignant lesion the age distribution ranged from 50 to 79 years with 15 cases (93.75%) seen in males (n=15) and only 1 case (6.25%) seen in female (n=1) accounting for male to female ratio of 15:1. Most of the malignant lesions were seen in an age group between 35 to 75 years with 51 cases (60.71%) seen in males (n=51) and 33 cases (38.29%) seen in females accounting for male to female ratio of 1.5:1. The mean age for premalignant lesions were 60.4 years and for malignant lesions were 54.6 years. Standard deviation was 9.350. In both premalignant and malignant lesions, the peak incidence was seen in 6th decade.

Among the malignant lesions 43% were smokers. Pan or gutkha were the most common form of smokeless tobacco and were consumed by 30% in the present study. Chewing and smoking tobacco were the next common form of consumption of tobacco which were seen in 18% of cases. 2% of the patients were consuming alcohol and 2% of the cases were smoking or chewing tobacco and consuming alcohol. The remaining 5% of the cases did not have any habits.

The most common habit in females in the present study was chewing pan which accounted to 85.29%. Females without any habits accounted to 5 cases (14.70%).

Smoking was the commonest habit both in premalignant and malignant lesions amounting to 81.25% & 35.71% respectively, followed by smokeless tobacco (pan/ Gutka) in 12.5% cases and 33.33% cases respectively.

Out of 100 cases in the present study, most common presentation was an ulceroproliferative growth which was seen in 76 patients, ulcerative growth was the next commonest seen in 12 cases. 11 cases presented with white patches, and only 1 case presented with red patch. The most common site of involvement in both premalignant 75% and malignant lesion 38.09% of the oral cavity was buccal mucosa followed by lateral border of the tongue (28.57%).

Amongst the premalignant lesions, Leukoplakia accounted to 93% of cases in the present study. Leukoplakia with mild dysplasia was common lesion accounting to 50% of the cases (Figure 1a) showing dysplastic cells with altered cellular polarity occupying lower 1/3rd, followed by moderate dysplasia in 18.75% cases (Figure 1b), showing dysplastic cells upto middle 1/3rd of the epithelium. Severe dysplasia was seen in 12.50% (Figure 1c) where dysplastic cells occupy upto upper third of the epithelium, show abnormal keratinisation of individual cells at all levels with nuclear changes. Numerous mitoses were also seen. CIS (Figure 1d), where the neoplastic cells occupying the full thickness of the epithelium and display nuclear changes and numerous mitoses and Hyperplasia displaying epithelial thickening, orderly progression of cellular maturation with absence of cytological atypia (Figure 2a) were seen in 6.25% cases each.

Among all the malignant lesions of the oral cavity, squamous cell carcinoma was the commonest type accounting for majority of the cases (94.04%). Among the remaining cases, Verrucous carcinoma and

basaloid squamous cell carcinoma accounted for 5.95% and 1.19% respectively. Grading of the malignant lesions were done which showed majority of the cases as well differentiated (49%) followed by 37.97% as moderately differentiated and 2.53% as poorly differentiated.

Staging of the tumours were done for all the resected specimens. Out of 11 resected specimens, 27.27% of cases belonged to T1N0M0 (Stage I), 18.18% of cases each belonged to T2N1MO & T2N0M0 (Stage II), 9% of cases belonged to T3N0M0. 9% cases each belonged to T2N2M0, T4N0M0 & T4N2AM0 (Stage IV). 36.63% cases belonged to high risk stage III and IV. 63.63% cases belonged to low risk stage I, II.

In the present study 27.27% resected cases showed perineural invasion and 18.18% cases showed microvascular invasion. The resected margins were uninvolved in all the 11 cases (100%).

Discussion

The commonest age group for premalignant lesion was 50-59yrs (62.5%). Present study is in concordance with Mehrotra R et al [1] and Dietrich et al [6] Majority of the patients with malignant lesions were in an age group of 50-59 years (41.66%). Present study was in concordance with Mehrotra R et al [7], Dhar PK et al [8], Misra V et al [9], Kandekar SP [10], Dragomir LP [11] et al. According to most of the studies, majority of the malignant lesions of the oral cavity are seen in patients over 50 years of age. Our study is found to be in concordance with many other studies which has similar findings. Hence, screening programs targeting men over 50 years, would help in early diagnosis of oral malignancy and therefore likely to improve the treatment outcome.

In the present study, there is a male preponderance for both premalignant lesions and malignant lesions accounting for 93.75% and 60.71% of cases respectively. All the studies conducted in India as well as other countries observed that oral cancer affects men more than women.

However, gender per se is not a risk factor in oral malignancies [12]. The incidence of oral malignancy is higher in males probably due to the higher rate of tobacco and alcohol consumptions. When compared to males' females in our society usually do not indulge in smoking although we are seeing a rising trend [13].

In our study, out of total 100 patients, smoking is the most common addiction seen in 43% of the cases and smokeless tobacco in the form of pan consumption was the only addiction amongst the female patient amounting to 85.29% of the cases. A study by Iype EM et al [14] and Durazzo MD et al [15] showed tobacco smoking as the commonest addiction identified in 80.8% of patients.

Amongst various locations for premalignant lesions, majority of cases of premalignant lesions were seen in Buccal mucosa (75%). Our study was in concordance with the findings of Mishra Met al [16], Lee J J et al [17], Misra V et al [2]. The most common location for malignant lesions in the present study was the buccal mucosa amounting to 38.09% in concordance with the study by Liu W et al [18], Ahluwalia et al [19], Sankaranarayanan R et al [20], Richard M et al [21]. Various published literatures show anatomically more anterior parts of the oral cavity frequently (anterior 2/3rdof the tongue, alveolus, lips, buccal mucosa and base of tongue) involved in oral malignancies. Prolonged contact of the anterior parts of oral cavity with the carcinogens present in tobacco and alcohol is probably the reason for it.

Out of the 15 clinically diagnosed cases of leukoplakia, only one case was diagnosed as leukoplakia without dysplasia (leukoplakia with hyperplasia). Remaining 14 cases were diagnosed as leukoplakia with dysplasia. Study by Bhattacharjee A [22] and Allegra E [23] et al was in concordance with the present study and revealed that the most common premalignant lesion was mild dysplasia (26.6%)

In the present study erythroplakia (Figure 2b) was less frequently seen and amounted to only one case (6.25%) and it was associated with mild dysplasia.

In the present study majority of malignant cases were Squamous cell carcinoma with various grades of differentiation amounting 92.87%.

Present study was in concordance with all the above studies which showed squamous cell carcinoma as

Table 1: Comparative analysis of histopathological spectrum of malignant lesions

Sl. No.	Authors	SCC	VC	Others
1.	Bhattacharjee et al[22] (2006)	85.12%	-	14.82%
2.	Khandekar et al[10] (2006)	72.5%	27.5%	-
3.	Diaset al[24] (2007)	93.9%	0.5%.	5.6%
4.	Brandizzi D et al[26] (2008)	91%	7%	2%
5.	Present study	92.87%	5.75%	1.19

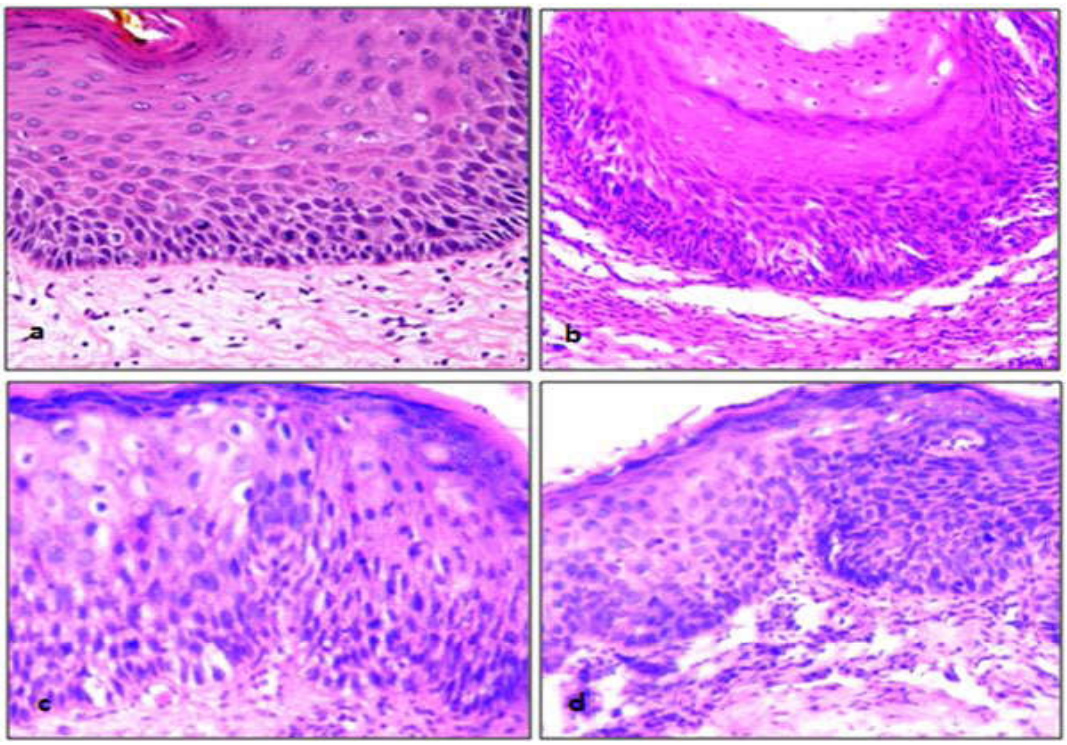

Fig. 1(a): Photomicrograph of leukoplakia with mild dysplasia showing dysplastic cells with altered cellular polarity in the lower one third of the epithelium. H&E 200X. **(b)** Photomicrograph of leukoplakia with moderate dysplasia showing dysplastic cells up to the middle one third of the epithelium. H&E 200X. **(c)** Photomicrograph of leukoplakia with severe dysplasia showing dysplastic cells occupying upto upper one third of the epithelium. H&E 200X. **(d)** Photomicrograph of carcinoma in situ showing dysplastic cells involving the full thickness of the epithelium. H&E 200X

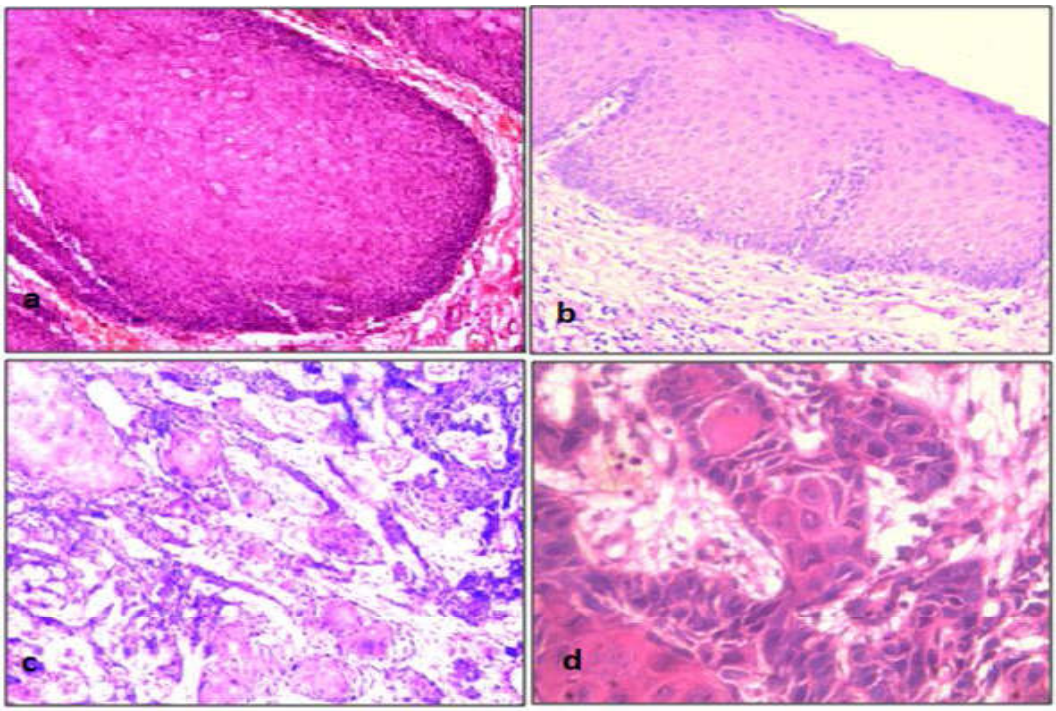

Fig. 2(a): Photomicrograph of leukoplakia with hyperplasia showing epithelial thickening. H& E 100X. **(b)** Photomicrograph of Erythroplakia with mild dysplasia. H & E 100X **(c)** Photomicrograph of well differentiated squamous cell carcinoma showing nests of tumor cells H&E 100X **(d)** Photomicrograph of well differentiated squamous cell carcinoma showing nests of tumour cells displaying individual cell keratinisation with preserved intercellular bridges. H&E 400X

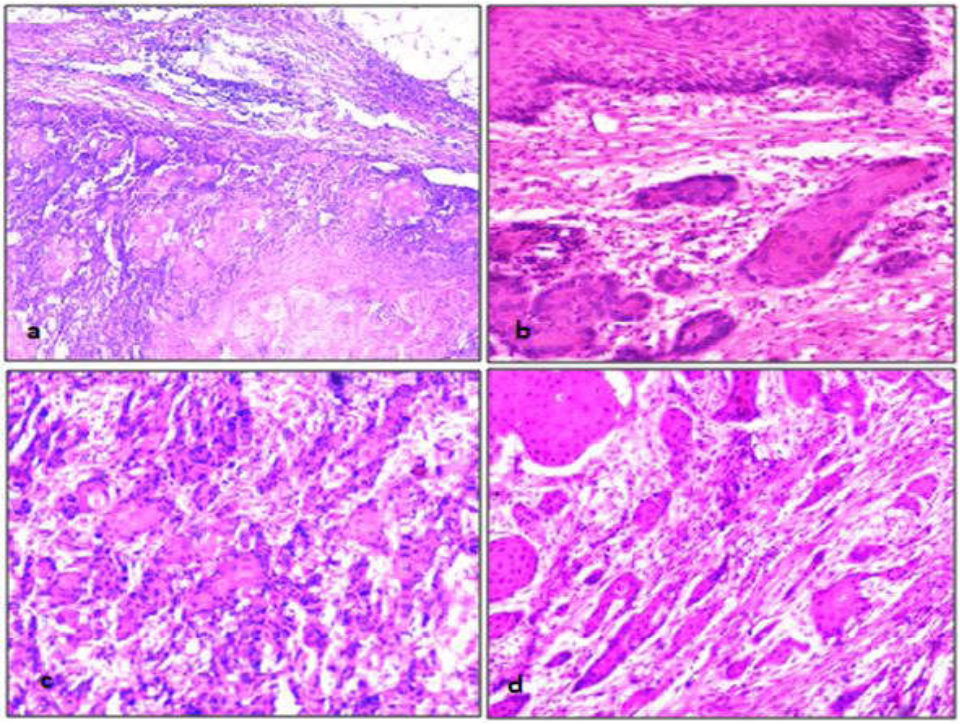

Fig. 3(a): Photomicrograph of well differentiated squamous cell carcinoma showing lymph node metastasis. H&E 200X **(b)** Photomicrograph of moderately differentiated squamous cell carcinoma showing nests of tumour cells 200X **(c)** Photomicrograph of moderately differentiated squamous cell carcinoma showing nests of tumour cells. H&E 200X **(d)** Photomicrograph of moderately differentiated squamous cell carcinoma showing pattern of invasion predominately in cords and islands. H&E 200X

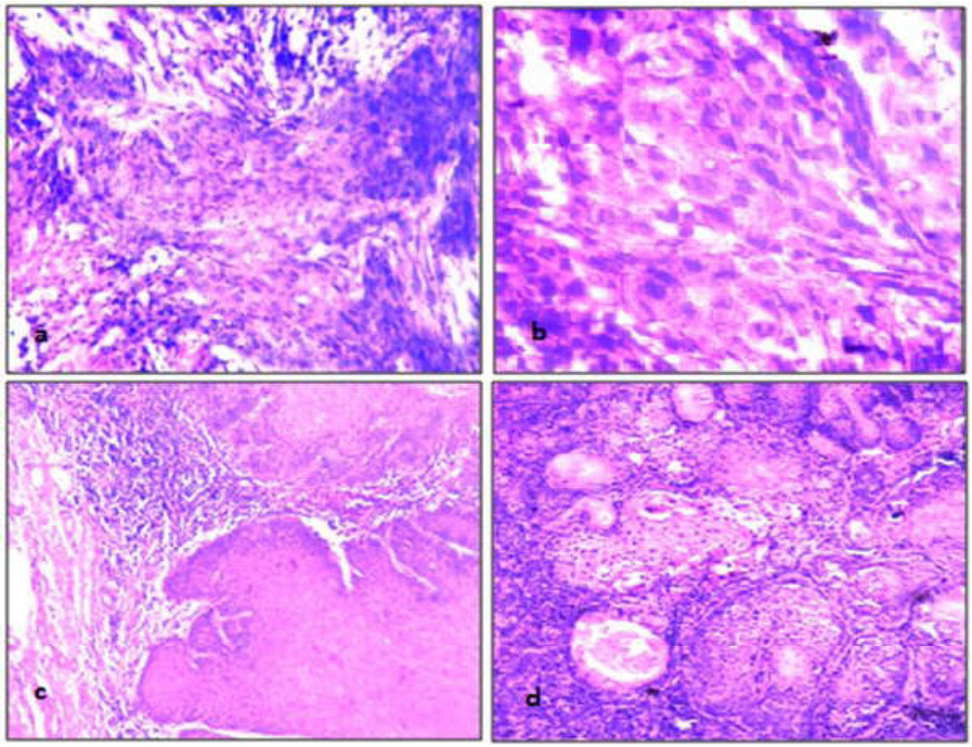

Fig. 4(a): Photomicrograph of poorly differentiated squamous cell carcinoma. H & E 100X **(b)** Photomicrograph of poorly differentiated squamous cell carcinoma H&E 200X. **(c)** Photomicrograph of Verrucous carcinoma showing broad blunt rete pegs with a pushing margin. H&E 100X **(d)** Photomicrograph of Basaloid squamous cell carcinoma showing lobular basaloid growth pattern. H& E 200X

the commonest histological type.

All the five cases (5.75%) of verrucous carcinoma (Figure 4c) displayed well differentiated squamous epithelium with surface of the epithelium showing prominent parakeratosis and are arranged in invaginating folds. The downward growth of the epithelium was broad, with blunt rete pegs, a pushing margin infiltrating at the same level with the advancing edge of the squamous epithelium exhibiting minimal cytologic atypia and mitotic activity. The lamina propria was composed of lymphoproliferative inflammatory cell infiltrate.

A single case of basaloid squamous cell carcinoma (Figure 4d) was seen in the present study which showed lobular, basaloid growth pattern predominantly with abrupt foci of squamous differentiation and prominent mitotic activity. The small basaloid cells had moderately pleomorphic densely hyperchromatic nuclei with scanty cytoplasm and the basaloid component at the periphery showed nuclear palisading and singlecell necrosis.

In the present study, the tumour differentiation was based on Broder's grading. Majority of the oral squamous cell carcinoma were well differentiated (60.25%). Sheets and nests of tumour cells with large hyperchromatic nuclei (Figure 2 c &d) and the presence of individual cell keratinisation with keratin pearl formation were the prominent features of well differentiated SCC which were consistently seen in almost all the cases. Another important feature is the intercellular bridges which were seen in 59.5% cases. Only 14.8% cases showed atypical mitoses. The pattern of invasion was predominantly pushing type in 59.5% cases, bands in 40.4% cases. Stromal lymphoplasmacytic infiltrate is seen in many cases.

SCC with moderate differentiation [Figure 3 b,c,d] showed nuclear pleomorphism with decrease in individual cell keratinization and absence of keratin pearl formation.The pattern of invasion was predominantly in bands, cords and islands with a few cases showing invasion with pushing pattern.

Poorly differentiated SCC [Figure 4a & b] showed predominantly immature cells with numerous atypical mitosis with absence of individual cell keratinisation, intercellular bridging and keratin pearl formation. The tumour cells showed lack of cohesiveness. The pattern of invasion was seen predominantly in single cells, cords and islands.In comparison with the various published literature, Ahluwalia et al [19], Patel MM [24] and Iype EM et al [14] our study was concordant with the above-mentionedstudy.

Out of the 11 primary resected specimens, 36.36% cases belonged to high risk stage (III and IV) and Low risk stage-I and II were seen in 63.63 % of the cases. Comparing with a study done by Jerjes et al [25] majority of the cases (75%) were diagnosed with T1/ T2 N0 tumours in contrast to a study by Iype et al [14], where oral cancers presented in advanced stage (stage III and IV) in 66.3% cases.

Increased tumour size has been associated with cervical lymph node involvement [Figure 3a], high recurrence rate and poor prognosis. Worse prognosis is expected in patients with nodal disease [25].

In the present study 27.27% of resected cases showed perineural invasion which is considered an ominous prognostic sign and has been shown to correlate with an increased incidence of regional lymph node metastasis,local recurrence and decreased survival.18% cases showed microvascular invasion.

In the present study, out of 11 resected specimens with neck dissections, 100% cases showed tumour clearance with negative margins of more than 0.5cms. Jerjes et al [25] study showed a tumour clearance of 93% cases. Lesional tissue within 0.5cms of surgical margin is associated with 80% incidence with recurrent disease.

According to the UK guidelines, margin is clear if both mucosal and deep margins are 5 mm and more. It is considered close if margins are 1-5 mm and margins of less than 1 mm are considered involved. Increase in local recurrence are associated with positive or close margins and have a negative effect on survival. Furthermore, several studies have shown that local recurrence and overall survival benefit can be achieved by the negative resection margins [26].

Conclusion

In a developing country like India, oral and oro-pharyngeal carcinomas are the most common malignancies. The high incidence of oral squamous cell carcinoma is due to the popularity of paan/ tobacco chewing and smoking addiction in this region. A premalignant lesion is like a smoldering volcano, which if not taken care of, may erupt, often with disastrous consequences.

A detailed clinical work up with histology can help in diagnosing more than 95% of oral cavity premalignant lesions and thus potentially reducing morbidity and mortality subsequent to malignant transformation. The current histological gold standard is the presence of epithelial dysplasia on a tissue biopsy, an important marker of malignant change & grading using WHO criteria.

The present study on 100 oral cavity lesions revealed predominance of malignant lesions and with only a handful presenting in premalignant stage. This study noted a late age of presentation of premalignant lesions. This delay could be explained by numerous factors in rural and semi-urban Indian population such as ignorance, delay in seeking medical attention and lack of medical facilities and access to specialist care. Hence in such a scenario detection of premalignant lesions is the exception and most of the patients present only after progression to full blown malignancy. Therefore, in high incidence areas in the presence of predisposing factors clinicians and pathologists alike should exercise a high degree of clinical suspicion. Patients should be evaluated with vigilance and meticulously screened to identify the disease in early stage, which is perhaps the only way to ensure a better prognosis.

References

1. Mehrotra R, Gupta A, Singh M and Ibrahim R. Application of cytology and molecular biology in diagnosing premalignant and malignant oral lesions. Molcancer 2006;5(11):476-498.
2. Mishra V, Singh P A, Lal N A, Agarwal P, Singh P. Changing patterns of oral cavity lesions and personal habits over a decade: Hospital based record analysis from Allahabad. Indian J Community Med. 2009;34 (4):321-325.
3. Neville B.W and Day T A. Oral cancer and precancerous lesions.Cancer JClin. 2002;52:195.
4. Ramaesh T, Mendis B.R.R.N, Ratnatunga N, Thattil R.O. Diagnosis of oral premalignant and malignant lesions using cytomorphometry. OdontoStomatol Trop. 1999-N85.
5. Poh C. F, Samsung Ng, Berean K, Williams P.M, Rosin M P, Leie Zhang L. Biopsy and Histopathologic Diagnosis of Oral Premalignant and Malignant Lesions. JCan Dent Assoc. 2008;74(3)283-8.
6. Dietrich AT, Reicharta PA, Scheifelea C.Clinical risk factors of oral leukoplakia in a representative sample of the US population. Oral Oncol. 2004;40:158–163.
7. Mehrotra R, Singh M, Kumar D, Pandey AN, Gupta RK, Sinha US. Age specific incidence rate and pathological spectrum of oral cancer in Allahabad. Indian J Med Sci. 2003; 57(9):400-404.
8. Dhar PK, Rao TM, Nair NS et al. Identification of risk factors for specific subsites within the oral and oropharyngeal region- a study of 647 cancer patients. Indian J cancer 2000;37:114-122.
9. Mashber A and Meyer H. Anatomical site and size of 222 early asymptomatic oral squamous cell carcinomas. Cancer 1976;37(5):2149-57.
10. Kandekar SP, Bagdey PS, Tiwari RR. Oral cancer and some epidemiological factors: A Hospital based study. Indian J Community Med. 2006;31(3):157-59.
11. Dragomir LP et al Clinical, epidemiological and histopathological Prognostic Factors in Oral Squamous Carcinoma. Current Health Sci J. 2010;36(4):1-9.
12. Dias GS, Almeida AP. A histological and clinical study on oral cancer: Descriptive analyses of 365 cases. Med Oral Patol Oral Cir Bucal. 2007;12(7):474-8.
13. Silverman S, Gorsky M, Lozada F. Oral Leukoplakia and malignant transformation: A follow up study of 257 patients. Cancer 1984;53:563-68.
14. Iype EM, Pandey M, Mathew A, Thomas G, Sebastian P, Nair MK. Oral cancer among patients under the age of 35 years. J postgrad Med. 2001;47(3):171-6.
15. Durazzo MD, Araujo CEN, Brandao Neto JS, Potenza AS, Costa P et al. Clinical and epidemiological features of oral cancer in a medical school teaching hospital from 1994 to 2002: increasing incidence in women, predominance of advanced local disease, and low incidence of neck metastases. Clinics. 2005;60(4):293-8
16. Mishra M, Mohanty J, Sengupta S, Tripathy S. Epidemiological and clinicopathological study of oral leukoplakia. Indian J. Dermatol. Venereol. Leprol. 2005;71(3):161-65.
17. Lee JJ, Hung HC, Cheng SJ, et al. Carcinoma and dysplasia in oral leukoplakias in Taiwan: Prevalence and risk factors. Oral SurgOral MedOral PatholOral Radiol Endod. 2006;101(2):472-480.
18. Liu W, Wang YF, Zhou HW, Shi P, Zhou ZT, and Tang GY. Malignant transfornmation of oral leukoplakia: a retrospective cohort study of 218 Chinese patients. Cancer. 2010;10:685
19. Ahuwalia H, et al. Spectrum of head and neck cancers at Allahabad. Indian J Otolaryngol Head Neck Surg. 2001;53(1):16-21.
20. Sankaranarayana R, et al. Effect of screening on oral cancer mortality in Kerala, India: A cluster randomised controlled trial. Lancet. 2005;365:1927-33.
21. Richard M, Kunnambath R, Risto S. et al. Role of tobacco smoking, chewing and alcohol drinking in the risk of oral cancer in Trivandrum, India: A nested case-control design using incident cancer cases. Oral oncol. 2008;44:446-454.
22. Bhattacharjee A, Chakraborty A, Purkaystha P. Prevalence of head and neck cancers in North East – An institutional study. Indian J Otolaryngol Head Neck Surg. 2006;58(1):15-19.
23. Allegra E, Lombardo N, Puzzo L, Garozzo A. The usefulness of toluidine staining as a diagnostic tool for precancerous and cancerous oropharyngeal and oral cavity lesions. Acta Otorhinolaryngol Ital. 2009;29 (4):187–190.
24. Patel MM and Pandya AN. Relationship of oral cancer with age, sex, site distribution and habits. Indian J Pathol Microbiol. 2004;47(2):195-197.

25. Jerjes W et al. Clinicopathological parameters, recurrence, locoregional and distant metastasis in 115 T1-T2 oral squamous cell carcinoma patients. Head Neck Oncol. 2010;2(9):1-11.

26. Brandizzi D, Gandolfo M, Velazco ML, Cabrini RL, Lanfranchi HE. Clinical features and evolution of oral cancer: A study of 274 cases in Buenos Aires, Argentina. Med Oral Patol Oral Cir Bucal. 2008;13(9):544-8.